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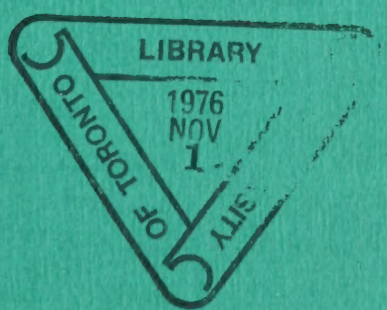
TRANSACTIONS

OF

THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE



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ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE
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Proceedings of a Meeting of the Society held on Friday, May 21st, 1920, at 8.30 p.m., at 11, Chandos Street, Cavendish Square, W. 1., Professor W. J. R. SIMPSON, C.M.G., M.D., F.R.C.P. (*President*), in the Chair.

THE ETIOLOGY OF PELLAGRA FROM THE STANDPOINT OF A DEFICIENCY DISEASE.

BY EDWARD J. WOOD, S.B., M.D., D.T.M. (ENG.).

In spite of the tremendous amount of work done in the study of the etiology of pellagra, it must be reluctantly admitted that the solution of the problem is not yet accomplished. It is, however, encouraging to note the great interest which has been aroused, and the high type of scientific research which is being brought to bear on its solution. The Great War has stimulated the interest of a number of brilliant investigators, who were given ample opportunity for the study of the disease, especially in Egypt. It would seem highly improbable that the addition to the field of research workers in pellagra of the large number of British investigators whose interest was aroused in Egypt, could result in anything but an early solution of a problem which has vexed Europe since 1735, and which during the past decade and a half has taken such terrific toll in the United States.

My only justification for appearing before this Society to discuss the question of the cause of pellagra lies in the hope that it may help to form a link in the chain of evidence, ultimately to result in a solution, for all my observations were made in the southern states of the United States, and chiefly in the State of North Carolina, where conditions of living and general hygiene are far different from those encountered by the British observers in Egypt. It is reasonable to presume that light may be thrown on the subject by a consideration of its occurrence in areas so widely separated.

I ask your indulgence in a rapid review of some of the more important work done in the United States and the more recent Egyptian reports.

It is interesting to note that there was no reference to the occurrence of pellagra in America until about 1907,[1] though an occasional case was reported of a sporadic nature.

Careful consideration of the matter convinces me that it is a great error to assume that the disease has existed in that country unrecognised for many years. I saw my first cases in 1905, and took great care to consult the older physicians in the fields of its occurrence to learn if they had ever seen it, but it was as strange to them as it was to me. It is, further, a notable fact that from 1905 to about 1909, the disease assumed a very malignant and fulminating type. Since that time it has gradually assumed the character of the chronic process described in Italian literature. This fact cannot but recall to one's mind the story of the visit to the Fiji Islands from Australia in 1875 of H.M.S. Dido, with measles aboard. According to the account of Sir WILLIAM OSLER, 40,000 out of 150,000 population died in four months. It was presumed that this was virgin soil for measles, and that since that time the death-rate has gradually approached the usual normal. Certainly, a like state of things occurred with pellagra, as I saw it in North Carolina in those earlier years, while to-day it differs little from the Italian type of the disease. This single point has been a continual obstacle in the way of accepting any view which excluded an infectious element.

In all the recent work done in the study of pellagra from a standpoint of a food deficiency, it must be admitted that there is still lacking an entirely satisfactory explanation of the seasonal incidence of the original outbreak as well as the recurrences. Dr. SAMBON[2] has presented some very strong points in favour of a short period of incubation which cannot be overlooked or fail to receive the most serious consideration. His carefully recorded instances of such cases as that of the parents in a pellagrous district suffering from the disease, their removal to a non-pellagrous district where non-pellagrous children were born, and the subsequent return after some years to the pellagrous district which was followed by the appearance of the disease in the children, could only be ignored by the prejudiced.

JOBLING and PETERSON[3] studied pellagra in the city of Nashville, Tennessee, and concluded that there was a connection between the incidence of the disease and poor sewage disposal. Their conclusions suggest that a lack of screening and the part played by flies could not be ignored, though they emphasised the fact that the pellagrous class consumed relatively more carbohydrate and less protein than is required to make up a properly balanced ration.

The THOMPSON-MCFADDEN[4] Pellagra Commission made its observations in Spartanburg County, South Carolina. They concluded the disease was in some way related to a bacteriological infection, and they, too, regarded the disposal of human excreta as playing an important part.

The work of JOSEPH GOLDBERGER,[5] with which you are doubtless familiar, has for its basis (1) that pellagra is essentially of dietetic origin; (2) that it depends on some undetermined error in a diet with a disproportionately high vegetable component and a disproportionately low protein component derived from animal or leguminous sources; (3) that no pellagra developed in those who consumed a mixed, well-balanced diet which is suitably varied. In an orphanage, GOLDBERGER found 75 per cent. of the children pellagrins in 1913, and the ones who escaped were the younger children whose diets were supplemented with cow's milk. His suggestions of a diet reform were adopted, and in 1914, in the same institution, among 234 inmates there did not occur a single case. He then selected what his experimental work indicated to be a faulty diet, and by an arrangement this diet was given to prisoners. Every effort was made to exclude all possible sources of error based on the various theories of etiology. A careful survey indicated that the only source of hygienic error rested in the diet. Resulting from this feeding experiment, a number of the men developed a disease condition regarded by GOLDBERGER and clinicians who had seen much of the disease as real pellagra. It is only fair to state at this point that there was criticism raised by some of the opponents of a food origin of the disease, because the skin lesions of the subjects of the experiment were on the scrotum rather than the exposed portions of the skin surface. This led me to review my cases of pellagra, and I shall shew you photographs which readily sustain the point that the covered portions of the body surface may be the seat of the lesion. In a number of cases I have found the skin lesions about the vulva, on the back, above and below the knees,

behind the knees, and, in fact, hardly a spot on the skin surface can be regarded as exempt from such a possibility. Too little attention has been paid to these atypical distributions, and it would be exceedingly unfair to discredit GOLDBERGER'S important work because of a lack of such knowledge.

GOLDBERGER then fed by mouth the fæces of pellagrins to a number of volunteers. In no case did anything suggestive of the disease appear as a result.

It is an important fact that in the United States the instances are neither single nor isolated where a dietetic reform in public institutions has resulted in a disappearance of pellagra, just as GOLDBERGER demonstrated.

W. H. WILSON,[6] in Cairo, has contributed importantly to the subject. He regards pellagra as due to a defective protein supply in the diet. His work resulted from careful analyses of diets known to have produced pellagra, and with others regarded as preventive or curative. He it was who directed attention to the biologic value of protein in such cases. The work of K. THOMAS[7] was depended on for the values of protein from various sources. To maintain nitrogenous equilibrium it was found that various substances differed widely. The biological value of vegetable protein, and especially that derived from maize, was found to be less than that of milk or meat protein. THOMAS estimated that the amount of tissue repair from 30 grams of meat or milk protein required 100 grams of maize protein to be equalised. It was thought that the inferiority of maize proteins could be explained by the large proportion of zein, which is devoid of both tryptophan and lysine, two amino-acids regarded as essential for animal nutrition. WILSON concluded that the danger from pellagra occurred when the biological value of the protein of the diet was below a certain point.

F. B. BOYD[8] and his co-workers studied pellagra in Egypt among prisoners of war. They found that the level of biological protein could be so exactly determined that they were able to anticipate the disease. Their work pointed strongly to the fact that a rest diet was inadequate to protect against pellagra when the victim was put to work. In their series 2,000 German prisoners, who supplemented the reasonably good prison diet in various ways, according to the well-known German appetite, escaped. But among 6,000 Ottomans, not so fortunate as to be able to have this supplement, 300 cases of pellagra developed in one year. It was found that if the disease was not far advanced it promptly responded to an increase in the biological protein value. These workers emphasised the importance of the part played by diarrhœal disease in disturbing the protein balance.

A recent summary of this Egyptian work shews that the absorption of protein from the intestines was less than 67 per cent., and that the metabolism of the Turkish prisoners of war is characterised by a low degree of assimilation of fat and nitrogen. At this point the justification of this communication seems apparent, for in my own work in America, on a carefully weighed Schmidt-Strassburger test diet, a normal utilisation of both fat and nitrogen occurred in pellagra, even in the terminal stages of a fatal case.

It has always, even since the days of CASAL, been a noteworthy fact that those living in the country districts were the victims of pellagra, while the urban population escaped. The Egyptian workers have proven, by careful analysis, that rural diets have lower values than urban diets, as there is a tendency for the agriculturist to send all his expensive animal foods to the better paid town dwellers and live chiefly on cereals. They suggested that the hill-man, depending more on his flocks for food, was more protected from pellagra than the valley-dweller, who largely depended on his cereal crop for his own sustenance.

A. D. BIGLAND,[9] in an admirable review of the whole subject, refers to the biological protein value of WILSON, as indicating the greater readiness with which meat protein is assimilated than the vegetable type. It is this assimilability which constitutes its biological value, and this point is placed by WILSON at 40 grams per diem. BIGLAND concludes that pellagra occurs most often in the underfed, speaking exactly, but may occur in the well fed. He speaks of the food deficiency being from without or from within. A comparison is made with perilobular cirrhosis of the liver, which may occur in the alcoholic but also in the non-alcoholic. This broader point of view may make possible an explanation of many of those baffling cases in which we have seen pellagra occur in the well-fed.

J. I. ENWRIGHT[10] reports on the occurrence of pellagra among German prisoners of war, who were given the very "fat of the land" in the way of food, and whose dietary, which is published in detail, will stand the closest scrutiny. In spite of such a diet definite pellagra occurred.

CHITTENDEN and UNDERHILL,[11] in the United States, produced a condition in dogs very suggestive of pellagra, on a diet which E. V. MCCOLLUM[12] found defective only in Fat-soluble A, and the latter's investigations on rats with the same type of diet resulted in failure to produce the pellagrous symptoms, but did bring about a retardation of nutrition and a condition approaching xerophthalmia. MCCOLLUM thinks there is good evidence that there occur sometimes cases of pellagra in individuals whose diets have included a certain amount of those things called by him protective foods, which include milk, eggs and leafy vegetables, and that the theory of infection is thereby supported. He thinks this view is supported by the occurrence of the disease in badly sewered districts.

Working under the suggestion of GOLDBERGER, after twelve years of a belief in an infectious nature of pellagra, I undertook to view it from the standpoint of beriberi. I was at once attracted by the report of P. A. NIGHTINGALE,[13] who had under his care the prisoners of a gaol in Rhodesia. These prisoners had always been fed on ropoko, a small cereal of the maize type, which was hand-ground by the prisoners, but owing to the failure of the crop they were forced to go outside and buy commercial "mealie meal," which seems to conform to the commercial corn meal of the Southern States of America. The result of this food change was a disease the description of which is accompanied by diagrammatic sketches, making the diagnosis unmistakable. Appreciating that the trouble was due to the change of food, NIGHTINGALE immediately abandoned the "mealie meal" for ropoko again, and, in his own language, the result was "immediate and magical." It is to be hoped that my hearers will appreciate the difference between this observation and the old maize theory of the early Italian School. In NIGHTINGALE'S observations there was no thought of toxicity but rather of a deficiency.

If pellagra is a deficiency disease, it may occur as often among those who eat wheat as among those who eat maize as the exclusive cereal diet. In either instance it is safe to say that milk, or other suitable animal protein, may readily offset the fault. So much impressed was I with NIGHTINGALE'S report, that I went to the maize-mill to learn how the grain suffered in the milling process. Briefly I[14] found that in modern steam-milling the grain was "degerminated," that is, it was deprived of the germ, which latter was ground separately, and, with the bran, sold as cattle-food, having a great reputation as a "milk maker." It will be recalled that the Philippine workers, in the experiments with polished rice, rice-polish and beriberi shewed that phosphoric acid (P_2O_5) was a reliable indicator of antineuritic substance. In my maize work the same plan was adopted. We found that the commercial germ product contained 1·15 per cent. of P_2O_5, while specially milled germ for experimental purposes often reached as high as 2 per cent. On the other hand, maize milled in the state of Ohio contained only 0·29 per cent. When the grain was ground *in toto* with no removal, according to the old plan, the P_2O_5 content was 0.78 per cent. The reason for the modern plan of milling is that the germ of maize contains so much fat that milling the grain without separating and removing this germ results in a product which early becomes rancid. The germ of maize is quite soft, and is poorly protected. If deterioration of an animal or vegetable source occurs, it is always the germ which suffers first and foremost. Is it not worthy of consideration that, if LOMBROSO had regarded pellagra as a deficiency rather than a toxicity, resulting from the destruction by the various moulds of the essential portion of the grain, a solution might have been reached? Substituting the word deficiency where he speaks of toxicity, makes his masterly work on the subject in close accord with many modern views. I then investigated the milling of wheat. It will be recalled that the antineuritc substance occurs in the cortical portion of the grain. Our analyses shewed that the bran portions of wheat contained 0·98 per cent. of P_2O_5, while average wheat contained only 0·14 per cent.

Experiments were undertaken on pigeons and chickens, having no point of originality except the substitution of deficient maize in place of polished rice in the production of

polyneuritis gallinarum. It was readily proven that the germ of maize contained the same property as the polish of rice. An alcoholic extract of the germ of maize was as effective in relieving the symptoms of polyneuritis as was the case with an alcoholic extract of rice polish. In the course of these experiments it developed that birds given grain, the phosphoric acid content of which was very gradually decreased, seemed to acquire a tolerance for the deficiency. But the young of these birds hatched from eggs laid during the experiment, while apparently free from polyneuritis at the hatching time, and continuing so until after leaving the nest, promptly became polyneuritic on the diet of the parent birds, though these latter remained free from any definite indication of the disease. Pigeons, on a diet of maize with a phosphoric acid content considerably below normal and yet not low enough to produce polyneuritis gallinarum, manifested droopiness, loss of feathers, and a red-legged condition which seemed quite distinctive. We have not yet dared to say that this condition is the analogue of pellagra as polyneuritis gallinarum is of beriberi. Pigeons fed on whole maize of the best quality were maintained in fair health, but without rapidity and extent of growth which would occur on a more natural diet. The condition of red legs was readily relieved by a substitution of good maize.

Repeating what has been done in the rice work in the Philippines by VEDDER and others, it was found that cooking the grain with sodium bicarbonate added materially to its deficiency.

I have cured polyneuritis gallinarum in the fowl by the administration of fresh cow's milk in almost as striking a manner as with the alcoholic extract of the antineuritic portion of the cereals.

Maize is frequently the bread cereal in pellagrous countries. The same experiments detailed above have been done with wheat. It is not then a question so much of the particular cereal as it is of the portion removed in the milling.

It would appear that the deficient portion of the several cereals in these experiments was the water-soluble B. The part played by milk, in my experiments in curing polyneuritis gallinarum, may have been due to the small fraction of water-soluble B, though it remains to be seen whether or not in pellagra the dietetic fault lies in the lack of one or both of these elements. The following experience illustrates the point. Applying the principle underlying NIGHTINGALE'S work, together with the suggestions derived from animal experimentation, I fed pellagrins with the germ of maize with notably prompt improvement. In one particular case the patient was *in extremis*, and was being fed by the tube. The food given in this way was eight ounces of fresh cow's milk, three eggs and one or two ounces of sugar of milk. There was no notable improvement until a gruel, made of wheat bran, was added, when at once the general condition of the patient greatly improved, though she eventually died the sudden death which I have so frequently noticed in this disease.

It is obvious that the pellagra class as a rule could never secure the expensive protein which would protect, regardless of the type of deficiency underlying the disease. Since this economic solution does not lie within our reach, it becomes the more important exactly to determine the type of dietetic fault, in order that it may be practically corrected with as little expense as possible.

Our experiments led us to suspect that the water-soluble B was more at fault by its lack than the more expensive fat-soluble A. Applying this suspicion practically, we have advocated the consumption of the whole cereal without the removal of a part in the milling and the cooking of the cereal without bicarbonate of soda as a rising agent. We found that the balance between acid and alkali in many baking powders was so crudely struck that for the present, at least, we are advocating that they be avoided. The results are already encouraging. Whenever possible, milk, fresh meat, vegetables and other sources of fat-soluble A are added.

If the problem is one simply of a too low protein level, or a too low biologic protein, there are many classes of sufferers that cannot be reached. If, however, we can finally determine that water-soluble B is the deficient element, it can be readily supplied at small cost. There is still much more work to be done before this matter is settled.

Many were impressed during the war with a belief that while beriberi may be a

deficiency disease, there must have been added an infectious element. One strong point along this line mentioned to me by a careful observer was the occurrence of jaundice. Surely, if this is a reasonable suspicion in the case of beriberi, the case of pellagra cannot be counted solved, at this time, especially in the light of such observations as those of ENRIGHT, JOBLING, the THOMPSON-MCFADDEN Pellagra Commission, MCCOLLUM, and finally, but probably most important of all, the epidemiological observations of SAMBON in Italy, Roumania, the United States and the West Indies. That nutritional errors do play a large part I do not doubt, nor do I believe that an individual on a well-balanced diet, especially when milk plays a part, will develop the disease, but I am unwilling at this time to exclude the possibility of an infectious element playing a part which may be secondary but no less essential.

In North Carolina, it was noticed that pellagra occurred chiefly in the foot-hills below the high mountains ; that, as a rule, along the Atlantic seaboard the incidence of the disease was much less. Our cotton mills are located in the foot-hills of the mountains, chiefly because of the water power so easily had there. In the high mountains the disease did not occur except very rarely. At one time it looked as though this distribution would coincide with the distribution of some insect pest, but such has not been demonstrated. There appeared to be a direct relationship between the lines of railroad travel and the occurrence of the disease. One might view this as an indication of an infection. On the other hand, I have observed that there seems to be a connection between the appearance of the disease and the introduction of such manufactured products as commercial maize meal and patent wheat flour, supplanting the old primitive plan of taking to the local water mill a small portion of maize, which was ground *in toto* and consumed before rancidity could occur. So far as a careful investigation of the manner of life of the people far removed from railroad travel and those living on the line of the railroad goes, the only real difference consisted in the manner of milling and cooking the cereal. The mountaineer in many instances violated every hygienic rule, and his diet was certainly not ideal, but he escaped the disease. On the other hand, the dweller in the foot-hills, working with all his family in a cotton mill, took whatever the local merchant provided and adopted all measures of shortening and making easy the cooking process. Consequently, the latter got wheat flour with no cortex, maize meal milled without bran or germ, and all manner of chemical rising agents. With this latter class, pellagra finds its greatest number of victims. It was interesting to trace the outbreak of pellagra in a village, timing its appearance with the abandonment of the old grist mill to which each farmer carried his small portion of cereal for primitive grinding. There seemed to be a striking coincidence in the appearance of the disease with the adoption of modern errors in milling and cooking.

The American pellagra problem differs from the Egyptian, essentially in the fact that diarrhœal diseases are relatively infrequent in the pellagra class. It is true that those infected with the *Necator americanus* fall an easier prey, and that we have much more amœbic dysentery than is usually thought, but, in spite of these exceptions, it must be granted that the element of chronic diarrhœa, so much stressed by the Egyptian workers, will not materially befog the atmosphere, and that the application of the Egyptian findings to our problem will be most helpful and instructive.

While the time has not arrived for a definite conclusion, we have found in North Carolina that, for all practical purposes, a careful analysis of each diet and a correction of its errors bring protection, and oftentimes relief.

I acknowledge with appreciation my debt to Captain GEO. F. CATLETT, of the United States Army, for great aid in the chemical portion of this work.

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DISCUSSION.

The PRESIDENT: Dr. WOOD, with his great experience of pellagra, has given us a very valuable and suggestive paper. He has examined the different views held in regard to the causation of the disease, and he has done it in a modest and scientific spirit. He has given credit to those who have worked seriously at the subject, while he has upheld his own views in a very convincing manner. This attitude is very different from that of a recent writer, who, I am afraid, does not quite comprehend the scope of the enquiry into pellagra instituted by the British Committee, and parodies the conclusions without apparently taking the trouble to study the reports connected with the investigation. Dr. WOOD, on the other hand, has made very important observations, and he shews, as many other investigators have, that the incidence of pellagra falls particularly upon those whose diet is at fault. He has shewn clearly, on the map and in the paper, that the incidence of pellagra in the country in which he has worked has fallen chiefly on the inhabitants who live on the foot-hills, and whose diet consists largely of wheat flour without the cortex, and maize that is milled and loses its germ. He also attaches very great importance—and has good reasons for it—to the fact that in using various chemicals for baking purposes, for the raising of the bread, the last straw is put upon the vitamines which may have been left. He differs from many observers in thinking that the water-soluble B is more important than the fat-soluble A; and certainly, if his views are correct, great economy will be practicable, whereas in the "no-protein" view there is likely to be a difficulty in practice owing to expense.

With regard to these nutritional diseases, we find that they are increasing largely in number. We now have, according to some, leprosy added, and tubercle as well We were always under the impression that these people were fed badly, but now we seem to be getting to the root of the matter as to the particular element which is wanting. But if leprosy and tubercle are deficiency diseases, they also have with them an infective element, and I am glad to see that Dr. WOOD does not lose sight of the fact of the extraordinary virulence of pellagra in its first invasion of his country. The sudden spread of the disease over a large part of the country is a matter which must not be lost sight of, and supports the view that there is some other agent associated with the deficiency element.

I take it this paper shews that the solution of the problem has not yet come—that it is necessary for further research to be carried out.

Dr. P. MANSON-BAHR: In the absence of Drs. BIGLAND and ENRIGHT, I have been asked to relate some of their extensive experiences of pellagra in Egypt, and to shew

some of the paintings of pellagra cases amongst German prisoners. I had the advantage of being associated with much of this work during my residence in Egypt. At first there was much to be said for the food-deficiency theory. The first pellagra patients we got in Egypt were Turkish prisoners from Arabia. Those who have followed the literature in the *Lancet* will have observed that, although some of us had our eyes open to the possibility of the occurrence of pellagra, we were at first completely mystified. In the first prisoners who came under observation, the only objective symptom was enormous œdema, which afterwards Dr. BIGLAND looked upon as analogous to the war œdema which was occurring in Europe. In January and February, 1916, some of these people commenced to have a typical pellagra rash. The evidence went to shew that, in some cases, these were recurrences of a long-standing disease, and that the œdema was an epiphenomenon. Most of the Turkish prisoners were affected with intestinal disease of some sort or other, and post-mortem bacillary dysentery lesions were common, though amœbic dysentery seemed to be rare. The low protein value of the diet and the scrappy existence these people had led in the last year or two seemed to favour the food-deficiency theory. In 1916 there was a serious outbreak amongst the Armenian refugees at Port Said, and that also could be explained on a food-deficiency basis. From the middle of 1917 onwards I had not the opportunity of following this subject further until the beginning of 1919, when, just after the Pellagra Commission had finished its work, out of the 7,000 Germans taken prisoner in Palestine the previous autumn, a considerable number started to develop typical pellagra, as you will see from the drawings. From January to June, 1919, when the observations ceased, there were sixty-five cases, that is, the disease occurred in approximately one per cent. of the German prisoners. Some were very ill, and, I think, one died. Nothing could be more typical than the distribution of the rash, even including the anomalous patches on the elbows, the inner side of the knees and the popliteal space. And, as far as one could make out, there was no reason to suspect that these men had ever suffered from any obvious food shortage. One outstanding fact was that two of the men were prisoners from German East Africa, who had been in prison camp at Maadi for two years—the very camp where the diet was favourably reported upon. Therefore, it seems we were up against a paradox. It may be said that the biological value of the protein was affected by the amount of the intestinal disease these men suffered from. But it will be seen that this is not the determining factor; they were not afflicted with malaria or dysentery more than our own men, and some of them were in the best possible condition, and on capture they looked remarkably healthy. One was a gymnastic instructor in the German army, and only had two months in Palestine previous to being captured.

The main difficulty to us was how to account for this outbreak of pellagra amongst apparently healthy Germans, who said they lived on "the fat of the land" while in Palestine—meat, fruit, milk and eggs, and who, a short period after their captivity, developed this disease, especially when they were thrown into close association with the Turks. That seemed to favour the idea of pellagra being an infectious disease. Considering the problem as a whole, how is it that, with all the food deficiency that existed in Central Europe during the war such as the distressing conditions in Austria, no epidemic of pellagra has been reported? And how is it that during the whole of the war, when our men have been in close association with natives who were known to be stricken with this disease—for instance, with the Egyptian Labour Corps, a proportion of whom were pellagrous—not a single case of pellagra has been reported as occurring among British troops, or amongst the hospital personnel who attended pellagrous Turks over a period of three years?

It seems to me that we have reached a critical stage in the investigation of pellagra. Perhaps too much is being made at the present time of deficiency in diets in general. Sprue and pellagra have many features in common. No one who has seen much pellagra and sprue can help being struck by the similar appearance of the mucous membrane and the tongue in the later stages, especially the similarity of the stools. From chemical and biological investigations it seems that the onus in those two conditions falls on the endocrine glands: in sprue, on the pancreas and the organs of digestion; while in

pellagra it would seem to be the suprarenals and the sympathetic nervous system in connection with those glands which bear the brunt of the process. There is also much similarity between Addison's disease and pellagra, and it seems that the branch of research which will bear more fruit at present than anything else is one which directs attention on the suprarenal gland. Is there some toxin acting specially on these glands, and is that toxin peculiar to the countries where pellagra occurs?

Lieut.-Colonel S. P. JAMES: I notice that although Dr. WOOD has added a lot of valuable information in support of the view that pellagra is a disease resulting from a faulty diet, he has not satisfied himself that it is the sole explanation. And he has told us that the food-deficiency theory does not account for the marked seasonal incidence which is the most striking feature in the epidemiology of the disease. I do not think anyone has been able to shew that in pellagrous districts the food varies materially with the seasons of the year, but, unless there are these variations, the faulty diet view is not a satisfying explanation from the epidemiological standpoint.

Dr. WOOD says there may be an "infective element," secondary to the food deficiency. If we admit that there must be two factors simultaneously at work to cause pellagra, is it necessary to say one of them is of an infective nature? Perhaps we are apt to dismiss too lightly the old idea of the effect of sunlight in causation. Dr. WOOD knows quite well that if one takes the statistics of South Carolina and plots them as carefully as one can, and then takes the hours of sunshine and plots them out, the apparent relationship between the two is remarkable The peak of the maximum sunshine is about a month before the incidence of pellagra. A similar relationship is apparent between sunshine data and pellagra incidence in Massachusetts and other States.

Lieut.-Colonel P. S. LELEAN: I have listened with very great interest to Dr. WOOD's paper, and also to Dr. MANSON-BAHR's remarks. As I had the privilege of working with Colonel BOYD on the Egyptian Committee of Enquiry into Pellagra, I think it would be unfair to him if I were to fail to point out certain facts, particularly in regard to the German prisoners.

With regard to the alternative theories of infectivity and food deficiency, it is interesting to consider the source of pellagra among Turkish prisoners of war. On very close investigation into the history of 440 cases among such prisoners—enquiries carried out by their own medical officers—it was found that only one of those patients had seen in his native home a corresponding rash, and only five had seen a similar rash among his acquaintances. Morever, thirty medical officers among the Turkish prisoners of war all denied that the disease existed in Turkey. Therefore, the occurrence of pellagra in the regions from which these men came was negligible. The first four cases of pellagra which could be traced among these prisoners had their initial attacks in Gallipoli. The troops were taken from there and passed to Syria, where similarly only a few cases (21) occurred—obviously among the very susceptible. What was the source of infection in Syria, if infection it was? Amongst the population there, medical officers who had had considerable experience in general practice stated that it was comparatively unknown, though they were acquainted with the description of it in the text-books. One had been fifteen years a practitioner in Damascus, but had seen only one case among the population there. When the Turkish troops came down into Palestine, pellagra came on in proportion as lengthened and overtaxed lines of communication led to failure in the supply of adequate rations. In captured documents we found evidence that their food was reduced to 67 per cent. of the authorised ration, and that it provided 24 per cent. less protein than is required for the performance of light labour, though they were engaged in arduous entrenching. Of these 440 cases which were closely investigated, the tabulated results shewing the onset of initial symptoms bore the following relation to the date of capture of these prisoners:—

12	to 6	months	before	capture	=	40 cases.
6	„ 0	„	„	„	=	279 „
0	„ 5	„	after	„	=	27 „
6	„ 12	„	„	„	=	13 „

If an infective origin is argued, how do you account for these figures, and for the fact that the men did not carry the power of infection into captivity? And why was the fall from 279 to 27 so sharply defined by the period of capture, *i.e.*, the passing on to a better diet? Remembering the indefiniteness of the initial symptoms, most of the dates of first onset must be regarded as recurrences.

We may further consider the evidence as regards infectivity which is afforded by an outbreak of pellagra in the Armenian refugees' camp on the Suez Canal. They were maintained in the same camp, with no change of site, and no altered range as regards biting-flies. There is no doubt that these people were subject to no materially altered condition, other than those of diet. After four months' exposure to a low diet, in which the biological value of protein varied from 22 to 27 grammes a day (adult male equivalent) they began to get pellagra in marked degree. Then the men went to work and got money, which they sent home, more food was purchased, and the pellagra rate fell. Then the men struck work and returned; they consumed the diet which otherwise their families would have found adequate, and up went the pellagra rate. The biological value of the diet in protein was raised above 40 grammes per diem (on the adult male standard), and coincidently with this increase the pellagra prevalence fell until it ultimately reached zero. There was subsequently no recurrence, although the people were living under the same conditions, except during a short period when there was a temporary diminution in their rations.

With regard to the German prisoners there is some difference of opinion. There was probably nobody in Egypt who had a more highly trained acumen for early cases of pellagra than Colonel F. D. Boyd. He had followed up many cases from the earliest diagnosis, and was able to detect pellagrins a month earlier in their development than were untrained or partly trained medical officers. He went down and saw those prisoners at Maadi Camp. Some had been there for over two years—since one of the enemy sea raiders had been run ashore in East Africa. They had not had a single case of pellagra during that year. Colonel Boyd examined 200 of these men, who were taken haphazard, and there was only one at whom it was necessary to take a second glance. The evidence is thus conclusive that at that time pellagra did not exist among those 2,000 German prisoners, although the 6,000 Turks in an immediately adjoining camp, and under precisely the same general conditions, were getting pellagra at the rate of 300 a year. We have just heard of pellagrous German prisoners "living on the fat of the land." Their authorised ration contained 54 grammes biological value of protein, 28·8 grammes of fat, and 351 grammes of carbohydrates, giving a total calorie value of 2,079—if this be "the fat of the land," the inhabitants thereof are not very gross feeders. As has been pointed out, the ratio of biological protein to the dietetic needs of the individual depends primarily on the extent to which it is assimilated, and, secondly, to its reaching the tissues. Here we had men who were only getting 2,000 calories, and the otherwise ample biological protein would not have reached their tissues, but would have been "deviated" to meet the immediate energy needs of the body, unless these had been met by augmentation of their ration by purchased food. The Germans were allowed two shillings a day, and, at the time of Colonel Boyd's inspection, they were augmenting their diet by practically the whole food value of that sum, so that their calories mounted up to 3,590. The essential point which must be considered is whether these Germans were at a later stage still receiving this money as Germany came nearer to bankruptcy. If not, they may have developed pellagra—as we should have expected—but they would certainly not have been living on "the fat of the land" at 2,000 calories a day; but, it must be remembered, that long-continued individual failures in assimilability may, in rare instances, determine an attack of pellagra by starving the tissues of protein, in spite of a most generous diet.

I owe it to Colonel Boyd that I should make these remarks, for he went into the investigation of these German prisoners with extreme care.

Dr. W. H. Willcox: The special point which interested me was Dr. Wood's attempt to supply a theory which would explain pellagra. I have not had the opportunity of seeing much pellagra, but the theories Dr. Wood put forward are exactly those which

have been advanced to account for beriberi. It was noted, in the cases which occurred in the Dardanelles and in Mesopotamia, that in addition to the deficiency in the diet, the water-soluble B element, there was an infective element. And in a paper I published, in 1916, on the relationship of jaundice to beriberi in the Dardanelles cases, this was pointed out. I would like to ask Dr. Wood to explain why, according to his theory, pellagra should develop, when, under the same conditions, viz., deficiency of water-soluble B element and an infective element, beriberi is well known to be caused.

If Dr. Wood's explanation of the cause of pellagra were correct, surely an outbreak of the disease will be associated with a number of cases of beriberi. There does not appear, however, to be any evidence of association of outbreaks of the two diseases, so that there must be a difference in heir etiology.

Mr. T. P. Beddoes: The great merit of the paper we have just heard, is that it presents such an admirable epitome of the various facts bearing on pellagra. What struck me most were the figures concerning the skin lesions. As far as one can see, it is possible the variation in the skin lesion depends on the degree of exposure to heat The lesions on the inner side of the knees may occur in those who live indoors and are in the habit of sitting facing the fire, with toes turned outwards, so that the affected part of the knee is that which comes quite near to the fire. That is the part which is frequently affected with chronic eczema, which may become so chronic that the skin is thickened, and it is then known as lichenization.

With regard to the cases of Dr. Goldberger, I ask whether my recollection of that paper is correct, that those men were kept in a separate building which was well shaded from direct sunshine.

As to seasonal incidence, we must remember that when pellagra was first recognised, the first characteristic lesions were skin lesions, and if they were absent, some hesitated to regard the case as pellagra at all. The next lesion was the intestinal one, producing disorders of digestion, and the third was the mental. The seasonal incidence which was reported depended on which of those disturbances was recognised as characteristic. A large number of advanced pellagra cases were found in lunatic asylums. Dr. Manson-Bahr has shewn that pellagra is now recognised at a much earlier stage than it used to be. One would like to know to what extent the lesions which occur on covered parts of the body are due to people living in the shade. Egypt, of all countries, is an unwooded country, whereas America is, perhaps, the most wooded country in the world.

With regard to the view that the sudden appearance and spread of pellagra in the southern states of America is in favour of infection, my recollection is that statistics in the *United States Health Bulletin* shew that the appearance of pellagra coincided with the spread of industrialism, causing decreased food production, decreased food values in the dietary from influx of population into the towns, in fact, that the rapid increase of pellagra is in favour of dietary deficiency and against the infection theory.

Dr. P. Manson-Bahr: I would like to assure Colonel Lelean I did not wish to criticize the Pellagra Commission report in any way. My only difficulty is that I cannot fit in all the recent facts with their conclusions. When I spoke of living on the fat of the land, I referred to the German prisoners who were taken in our last advance, not those who had been living in prison 13 months or more. The official German Army ration in Palestine which was given to Dr. Enright by the sergeant-major in charge of the ration dump at Damascus, was a very generous one: 750 grammes of bread per day, 453 of fresh vegetables, in addition to beans, rice, potatoes, and 350 grammes of fresh meat and 30 grammes of sausage, and sugar and coffee, milk and eggs. A striking fact was that one man developed pellagra after he had been only two months in Palestine before capture. He was five months in captivity before he developed a pellagrous rash, and quite a number of Dr. Enright's cases became pellagrous whilst in hospital suffering from other diseases, such as malaria or dysentery.

Lieut.-Col. P. S. LELEAN: In reply to Dr. MANSON-BAHR, the figures I gave were those of the official ration, and there is no reason to suppose they are inaccurate. It is the scale laid down by G.R.O I understood Dr. MANSON-BAHR to say that on the average prisoners had been in captivity three months. Our observations indicated that a four months' dietetic shortage preceded the outbreak of pellagra among the Armenian refugees. The case he has just quoted of the prisoner who had been in captivity five months, just brings him into the period at which one would expect pellagra to break out under a dietetic shortage, but one has to remember that the vast majority of cases reported as "fresh cases" of pellagra among prisoners of war in Egypt, proved on close enquiry to be recurrences. In 1919, the D.M.S., E.E.F., reported that of the "primary cases" investigated in that year, "Practically everyone has had previous symptoms and hospital treatment for the disease."

Dr. E J. WOOD: I have presented the case to you as I found it, without reservation. In some things I was able to form an opinion, while in many points the facts were left for discussion in the hope that light might be thrown on the difficult places I have received such a wealth of help in this study in London, that I hoped to be able to contribute to the work a small link in the chain from my American experience.

The idea of an infection is not mine, but it seems inexpedient to reject it until we have more conclusive proof. The Thompson-McFadden Pellagra Commission had the advantage over the Egyptian Commission, in that they were able to follow their cases through several years, and their conclusion is that the disease is an infection controlled by the proper disposal of sewage. Added to their work, is what we hear now from Major MANSON-BAHR, who corroborates ENRIGHT in the suspicion of an infection. In the idea of infection MCCOLLUM, too, is in accord.

Several years ago, Dr. JOSEPH GOLDBERGER came into the southern states teaching the doctrine of an insufficient protein diet. I had for several years represented the North Carolina State Board of Health, in this matter, and was convinced that the disease was an infection. Opportunity soon came to me to go over in detail with Dr. GOLDBERGER a long series of my own cases. At the end of this conference we agreed that I should view my next hundred cases from the beriberi viewpoint. This I did, and on leaving America I regarded the problem as solved, though not agreeing altogether on the nature of the deficiency. The admirable work of Professor BOYD and his associates in Egypt seems to me to be entirely in accord with the work of GOLDBERGER in America. Certainly their conclusions are identical.

In experimenting with pigeons and chickens I found that a diet deficient in water-soluble B, but not entirely lacking in it, resulted in a condition characterised by droopiness, loss of feathers and red legs. I am not prepared to say this was the analogue of pellagra, as polyneuritis is of beriberi. The beriberi nations are usually one-cereal people, and if that cereal is deficient, as in the case of polished rice, beriberi results. My own idea is that pellagra is the result of the same sort of deficiency, but less of it, because the pellagra people are not one-cereal consumers, but always supplement the grain with some other food.

In America, many of us regard the problem as solved, so far as prevention is concerned. Wherever GOLDBERGER'S views have been fairly applied, the disease has disappeared. It remains a question for solution, how can this be most practically accomplished? The famine stricken nations can hardly be expected to secure sufficient protein food. If, however, it can be proven that the less expensive water-soluble B is the vital factor, the problem is greatly simplified, for this can be supplied at small cost.

LABORATORY MEETING.

A Laboratory Meeting was held on 19th March, 1920, at the Royal Army Medical College, when the following microscopic preparations or apparatus were on view or demonstrated :—

1. "Rabies," by Sir STEWART STOCKMAN.
2. "The Amœbæ of Man," by Mr. CLIFFORD DOBELL.
3. "Some of the Pathogenic Fungi," by Colonel S. L. CUMMINS and Major J. C. PERRY.
4. "Development of Malarial Parasites in Mosquitoes," by Dr. C. M. WENYON.
5. "Trypanosomes outside Blood-vessels," by Dr. A. C. STEVENSON.
6. "Scurvy in Animals," by Surgeon-Capt. P. W. BASSETT-SMITH.
7. "The Agglutinometer," by Dr. GARROW.

REVIEW.

WAR AGAINST TROPICAL DISEASE.

We have received a copy of Dr. BALFOUR's new book, entitled *War against Tropical Disease.* A sub-title explains that it is a series of seven sanitary sermons addressed to all interested in tropical medicine and hygiene. All but one of these, "The Palm from a Sanitary Standpoint," have already been delivered as lectures, and have appeared in print. They have now been revised and brought to date.

It was a happy thought which led the author to collect his sermons in this beautiful volume It is written in his well-known interesting style, and without sacrifice of scientific accuracy the matter is presented clearly, and in such simple language that it is a pleasure to read the book. It cannot fail to appeal, not only to the sanitary expert, but also to the layman who desires to understand something of the fascinating problem of the War against Tropical Disease.

The first Sermon deals with the functions and duties of the Sanitary Inspector, that intermediary between the Medical Officer of Health and the native subordinates. The author is, of course, speaking of his experiences when Medical Officer of Health in Khartoum, where he found that without the British Sanitary Inspector it was impossible to carry out or enforce the regulations which were necessary. He describes the difficulties that had to be overcome, and the necessity of never-ceasing vigilance and labour. Even in most trying circumstances humour is not lacking, and we are told that, on one occasion, the Medical Officer of Health had to fine himself for the discovery by a Sanitary Inspector of a mosquito breeding-place in his own premises.

Sermon No. 2 is an account of the author's journey in the New World, where he visited Barbados, Grenada, Trinidad, Venezuela, Curaçao, Maracaibo, Colombia, Jamaica, Cuba and other places. As the author remarks, it is well on such occasions to be blessed with the sanitary eye, though the sanitary nose may not always be a pleasant possession. It is evident he had the former, from the fund of information presented to the reader. He describes the condition of the "poor whites" in Grenada, the descendants of the original white settlers who came from Barbados. They are ridden with malaria and ankylostomiasis, and he points to this as an opportunity for some wealthy philanthropist to save the offspring of these poor people. The author still wonders if the red howler monkey may not sometimes play a part in the spread of yellow fever.

Sermon No. 3 deals with preventive inoculation against typhoid and cholera, and is a lecture delivered under the auspices of the Research Defence Society early in the war. It presents, in an ingenious manner, the main features of protection of the human organism against bacteria.

The fourth Sermon is entomological, and deals with the noxious insects of Macedonia. It was given as a lecture there during the war, and did much to popularise the bearing of entomology on tropical medicine. Medical officers who served with that Force never forgot the lessons learned on this occasion.

Sanitary and Insanitary Makeshifts in the Eastern War Areas is the title of the fifth Sermon. It shews the wonderful ingenuity of officers in the field, who contrived to meet the sanitary requirements often when practically no material was available. The petroltins receive their deserved praise, and the author remarks that he cannot say where we should have been without these aids to hygiene. The persistence with which certain officers demanded material for sanitary purposes, is illustrated by the commanding officer

who could obtain no wood till he indented for a load of timber to erect crosses over graves. Wood there was for the dead but not for the living. A feature of this sermon is the numerous illustrations of sanitary contrivances.

The sixth Sermon deals with the problem of Hygiene in Egypt, the collected Chadwick Lectures delivered in 1919. The author was President of the Commission to enquire into the working and organisation of the Public Health Department of Egypt, and no one was better qualified to speak on this subject. The lectures review the whole of the sanitary conditions of Egypt, and indicate the lines along which improvements should be made.

The final Sermon, on the palm-tree from a sanitary standpoint, appears in this volume for the first time. It must come as a revelation to many that the palm-tree is so closely bound up with the life of man. One would almost think that if man and the palm-tree were left alone in the world he would still be able to house, clothe and feed himself in comfort, and live in a world which was still beautiful.

The foregoing is merely an outline of the contents of this most interesting and fascinating volume. No one who takes it up will find it dull—it is the very reverse of this. It is full of lessons for everybody interested in the welfare of mankind, and the motto of the book may be said to be that of the tireless Scarab, "Weary not in well doing," and illustrated in the charming little picture at the end of the entomological sermon.

The book is beautifully produced and fully illustrated. Many of the pictures are from the author's own photographs, taken during his sanitary wanderings in many theatres of war. The mere perusal of these alone is an education in itself. The Wellcome Bureau of Scientific Research is to be congratulated on being able to offer to the public, especially at this difficult time, such an interesting and instructive volume.

War against Tropical Disease: being Seven Sanitary Sermons addressed to all interested in Tropical Hygiene and Administration. By ANDREW BALFOUR, C.B., C.M.G., M.D., B.Sc., F.R.C.P. (Edin.), D.P.H. (Camb.), Director-in-Chief, Wellcome Bureau of Scientific Research. Published for the Wellcome Bureau of Scientific Research by Baillière, Tindall & Cox. Price 12s. 6d. net.

CORRESPONDENCE.

"THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE."

The following letter is published for the information of Fellows :—

402819. Home Office,
Whitehall, S.W. 1.
9th June, 1920

SIR,

I am directed by the Secretary of State to inform you that he has laid before the King your application of the 13th April last for permission to use the prefix "Royal" in the name of "The Society of Tropical Medicine and Hygiene," and that His Majesty has been graciously pleased to command that the Society shall be known as "The Royal Society of Tropical Medicine and Hygiene."

I am Sir, your Obedient Servant,

A. J. EAGLESTON.

The President, The Society of Tropical Medicine and Hygiene,
11, Chandos Street, Cavendish Square, W.

THE EDITOR, TRANSACTIONS OF THE SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

DEAR SIR,

It may prove of interest to those studying pellagra and the so-called deficiency diseases to briefly refer to results obtained in the treatment of a group of pellagrins, which were the subject of two papers by myself in the TRANSACTIONS of this Society.[1]

In 1912 were published some preliminary observations on pellagra occurring among the inmates of the Central Prison, Nyasaland, this being the first record of pellagra in Africa, apart from Egypt and the few cases observed by SANDWITH on Robben Island.

During 1913 the incidence of the disease was very much greater, and, in the second communication, the disease as then seen was dealt with at greater length from the clinical side, a number of observations bearing on the etiology of the affection were given, and the following statement made: "There are many reasons for supporting the possibility that pellagra is a deficiency disease . . . all 'maize' theories of causation as such are disproved." This conclusion having being arrived at, the next task was to effect an

alteration in the prison diets, which reference to previous papers will shew were ill-balanced and deficient in accessory food factors. A new scale of diet, which included maize, rice, green vegetables, beans, an oily fish (dried), and meat, was eventually put into effect, and proper cooking arrangements were provided.

Unfortunately, with the outbreak of war, I had to leave Nyasaland, and the exigencies of the military position prevented the previous records being kept up. I have recently, however, had the opportunity of communicating with Dr. ELDRED, the medical officer in charge of the Central Prison, during the war, up to the end of 1919, and he has informed me that since 1914 no new cases of pellagra had occurred among the inmates of the Central Prison, and that many of the early cases improved or were completely restored to health.

Excepting the change in diet all the other conditions remained the same, so that this small group of men, under exactly known conditions, have constituted a practical feeding experiment, and the results go far to confirm the hypothesis that an ill-balanced diet is an etiological factor in the causation of pellagra.

I regret that circumstances do not permit me to support these findings with analyses of the several dietaries concerned

The actual part played by the deficiency of accessory food factors in "deficiency diseases" is, I believe, not nearly such a simple problem as many writers would lead one to think. I believe it is very necessary to keep clearly before one the attitude that "the absence of something cannot produce anything." Rather should we consider the problem presented by any deficiency disease as one in which, in the absence of some controlling factor (the accessory food factor), other factors come into play.

We should not be content, as there is a tendency to be, to label such and such a disease a deficiency disease, but we should seek further and attempt to find the toxic substance which is directly responsible for the lesions. Such a substance may be one normally produced in the body, or the result of abnormal metabolism, or one produced as the result of an infection by some living virus, but one which remains "undetoxicated" in consequence of the absence of an accessory food factor, acting, possibly, by an upset of the balance of endocrinic secretion.

KINNIER WILSON[2] has published a preliminary paper on the pathological findings in the nervous system of thirteen cases of pellagra (nine of which were cases from Nyasaland), which have a very direct bearing on the problem of pellagra etiology.

The changes described are comparable to those found in cases clinically diagnosed as subacute combined degeneration of the cord, and WILSON has shewn that in pellagra the pathological evidence favours the idea that "an ascending toxic lymph stream invades the cord *via* the lumbar and dorsal posterior roots, and that the effects of the toxæmia appear either simultaneously in the nerves and cord or previously in the former, and that the toxin is probably of alimentary origin."

Yours faithfully,

HUGH S. STANNUS.

1. "Pellagra in Nyasaland." H. S. STANNUS. *Trans. Soc. Trop. Med. and Hyg.* Jan., 1912. Vol. V. No. 3.

   Ibid. Nov., 1913, Vol. VII. No. 1.

2. "The Pathology of Pellagra." S. A. KINNIER WILSON. *Trans. Neur. Sect. Roy. Soc. Med.* Jan., 1914.

LIST OF FELLOWS.

The following were duly elected Fellows of the Society:—

John W. Arthur, M.D., British East Africa.
W. M. Chambers, M.D. (Brux.), Kuala Lumpur.
W. E. Corbett, F.R.C.P. & S.I., Plymouth.
Major J. A. Cruickshank, M.D., I.M.S., Bombay.
G. A. Finlayson, M.B., M.R.C.P., Singapore.
Samuel Foskett, M.B., Harrogate.
Jenner Hoskin, M.R.C.S., London.
Major Robert Knowles, I.M.S., Calcutta.
J. C. G. Ledingham, C.M.G., Lister Institute.
Major P. J. Marett, M.R.C.S., R.A.M.C., Egypt.
Colonel W. H. Ogilvie, C.M.G., M.B., I.M.S., London.
Lieut.-Colonel S. E. Pratt, M.B., I.M.S., Karachi.
Major W. J. Simpson, M.B., I.M.S., Gilgit
Lieut.-Colonel F. H. Stewart, M.D., I.M.S.
R. G. White, M.B., Cairo.
Lieut.-Colonel E. Hasell Wright, M.R.C.S.E., I.M.S., North Coorg.
R. R. Scott, M.R.C.S., Daves Salaam.
G. R. C. Wilson, M.R.C.S., Tanganyika.
Lieut.-Colonel F. N Windsor, M.R.C.S., I.M.S.
Captain Neil Cantlie, M.C., R.A.M.C.

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